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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,683	11/15/2001	Avi J. Ashkenazi	P2730P1C32	4971

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,683	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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Detailed Action

Status of Application, Amendments, and/or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

In view of the papers filed 5 January 2005, the inventorship in this nonprovisional application has been changed by the deletion of: Avi, Askenazi, Kevin Baker, Luc Desnoyers, Dan L. Eaton, Napoleone Ferrara, Sherman Fong, Hanspeter Gerber, Mary E. Gerritsen, J. Christopher Grimaldi, Ivar J. Kljavin, Mary Napier, James Pan, Nicholas F. Paoni, Timothy Stewart, Daniel Tumas, Colin K. Watanabe, P. Mickey Williams and Zemin Zhang.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

The Response and Amendments submitted 12 May 2005 have been entered. Claims 1-118 and 124 are canceled.

Claims 119-123 are under examination in the Instant Application.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

Withdrawn Objections And/or Rejections

Continuity

The objection to the Specification for not complying with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119, is *withdrawn,* based on Applicant's arguments (page 3, 12 May 2005). The filing date of the Provisional Application (23 June 1999) is considered as the priority date.

Maintained/New Objections and/or Rejections

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 119-123 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under *35 U.S.C. § 101* are set forth at pages 4-10 of the previous Office Action (18 October 2005). Claims 119-123 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (18 October 2005), one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue (*Remarks/Arguments*, 12 May 2005, page 7 and throughout) that the data presented in the instant Specification are enabling for the cognate antibody of the polypeptide of SEQ ID NO: 351. They argue that the PRO1153 nucleic acid is a diagnostic marker for a variety of normal and cancerous tissues, and point to the results of the DNA

amplification assay (page 6, 12 May 2005).

Applicant's arguments (12 May 2005) have been fully considered but are not found to be persuasive for the following reasons:

In the instant case, the specification provides data showing a very small increase in DNA copy number- about 2.5 fold- in many types of normal and cancerous tissue, not just one kind of cancer (see Table 8). However, there is no evidence regarding whether or not PRO1153 mRNA or polypeptide levels are reliably increased in a cancer. Furthermore, as discussed in the previous Office Action (18 October 2005, page 9), what is often seen is a *lack* of correlation between DNA amplification and increased peptide levels (Pennica, et al; 1998, Proc. Natl. Acad. Sci., 95: 14717-14722). As discussed by Haynes et al (1998, Electrophoresis, 19: 1862-1871), polypeptide levels cannot be accurately predicted from mRNA levels, and that, according to their results, the ratio varies from zero to 50-fold (page 1863). The literature cautions researchers against drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2: 405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). Applicants dispute Hu et al's findings, stating: "Hu et al manipulated various aspects of the input data" (Response, page 6) and the "correlation was

only found among ER-positive (breast) tumors not ER-negative tumors" (Response, page 7). Applicants also point out that the Hu, et al data "may reflect a bias in the literature" (Response, page 7)." However, it is difficult to fault "bias in the literature" in the Hu article when the study simply aimed to compare message with protein for 2286 genes in breast cancer. And a discussion, by the authors, of the *possible sources* of error in an extensive survey study is not unusual in a well-crafted research paper. Regardless of whether there is a correlation between mRNA or DNA amplification and protein levels in a sample, the data presented in the instant Application do not show a consistent positive response even among the cancer samples.

Given the small increase in DNA copy number of PRO1153, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that a small increase in gene copy number would correlate with significantly increased mRNA or polypeptide levels. Further research needs to be done to determine whether the small increase in PRO1153 DNA supports a role for the antibody in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in Brenner v. Manson, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,

> "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the Specification's assertions that the claimed PRO1153 antibodies have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

There is no evidentiary support that PRO1153 is involved in the etiology of cancer in the many tumor samples and many normal tissues disclosed in the instant Application. Furthermore, as noted above, the increase in PRO1153 DNA in several normal tissues *and* several tumors of the *same tissue type* (see table 8) points away from its role in a disease. At any rate, a positive result rate of about 50% is too incomplete to make a conclusion about PRO1153 and cancer. The *specific* function of the PRO1153 polypeptide has not been disclosed by Applicants or by recent research.

As discussed in the previous Office Action (18 October 2005), a 2-fold (a few samples were greater) increase is not large and may be less likely to indicate disease (Hu, et al, 2003, Journal of Proteome Research 2:405-412), or may be sufficient (Applicant's Response, page 12). However, the type or magnitude of increase is not at issue in this case. All that is known about the PRO1153 peptide is that it is increased in some normal tissues and some cancerous tissues. It cannot be determined what the function of the protein is in the tissue; certainly the tissues provide no clues. It is hard to conceive of a specific and substantial utility for a protein for which so little consistent data or information is given. What might be the connection between the stained normal tissues and the stained cancerous tissues that would provide clues to the protein's function?

Because Applicants do not know the function of the PRO1153 polypeptide, *detecting* (by use of the claimed antibodies) the PRO1153 polypeptide has no specific function, since it is not useful to detect a protein for which a function has not yet been identified, and additionally might be expressed in several normal tissues and several cancers. Since the asserted utility for the PRO1153 antibody is not in currently available form, the asserted utility is not substantial.

Conclusion

No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about

the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
20 July 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER